

L Number	Hits	Search Text	DB	Time stamp
1	78	cln3	USPAT; US-PGPUB; DERWENT	2003/08/11 11:51
2	16	cln3 same (cancer\$6 or prolifer\$6 or overexpress\$6 or upregulat\$6)	USPAT; US-PGPUB; DERWENT	2003/08/11 11:53
3	5679	boustany-\$.in. or guo-\$.in. or amalfitano-\$.in.	USPAT; US-PGPUB; DERWENT	2003/08/11 11:54
4	364	(boustany-\$.in. or guo-\$.in. or amalfitano-\$.in.) and cancer	USPAT; US-PGPUB; DERWENT	2003/08/11 11:54
5	3	((boustany-\$.in. or guo-\$.in. or amalfitano-\$.in.) and cancer) and cln3	USPAT; US-PGPUB; DERWENT	2003/08/11 11:54

(FILE 'HOME' ENTERED AT 12:35:55 ON 11 AUG 2003)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 12:36:16 ON 11 AUG 2003

L1 1192 S CLN3
L2 118 S L1 AND OVEREXPRESS?
L3 17 S L2 AND (CANCER? OR PROLIFERATI?)
L4 7 DUP REM L3 (10 DUPLICATES REMOVED)
L5 205 S BOUSTANY R?/AU
E BOUSTANY R?/AU
L6 65 S E5-E6
L7 24 S L6 AND CLN3
L8 12 DUP REM L7 (12 DUPLICATES REMOVED)
E AMALIFTANO A?/AU


=>

L4 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:109700 BIOSIS
DOCUMENT NUMBER: PREV200100109700
TITLE: Blocking of **CLN3** expression by antisense
CLN3 adenovirus suppresses **cancer** growth
by modulating ceramide levels and delaying recovery from a
nocodazole induced G2M block.
AUTHOR(S): Rylova, S. (1); Jansen, P.; Amalfitano, A.; Pane, M.;
Boustany, R. M.
CORPORATE SOURCE: (1) Duke University Medical Center, Durham, NC USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No.
1-2, pp. Abstract No.-766.2. print.
Meeting Info.: 30th Annual Meeting of the Society of
Neuroscience New Orleans, LA, USA November 04-09, 2000
Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English


AB Juvenile Batten disease is a neurodegenerative disease. Accelerated
apoptotic death of photoreceptors and neurons occurs due to defects in the
CLN3 gene. **CLN3** has antiapoptotic activity when
overexpressed in NT2 neuronal precursor cells. We have shown
overexpression of **CLN3** in a variety of **cancer**
cell lines and solid colon **cancer** tissue: **CLN3** is
overexpressed in glioblastoma (U-373G, T98g), neuroblastoma
(IMR-32, SK-N-MC), prostate (Du145, PC-3, LNCap), breast (BT-20, BT-549,
BT-474), colon (SW1116, SW480, HCT 116) and leukemia (HL-60) cell lines,
but not in malignant melanoma or pancreatic **cancer** lines. An
adenovirus bearing antisense **CLN3** (Ad-AsCLN3) was used to
transduce BT-20, SW1116, T98g **cancer** cell lines and resulted in
blocking of **CLN3** expression as seen by Western blot. Also
suppression of **cancer** cell growth was seen by 3H-Thymidine
incorporation and cell counting. Ceramide levels were increased 52% after
transduction of DU145 prostate **cancer** cells with 40 MOI of
Ad-AsCLN3 virus. Neuronal precursor NT2 stable cell lines both over and
underexpressing **CLN3** were synchronized by blocking them at the
G2/M phase of the cell cycle using Nocodazole. The cells
overexpressing CLN3 rapidly exited G2/M and proceeded
through the cell cycle after removal of Nocodazole in comparison to NT2
cells underexpressing **CLN3** as seen by flow cytometry. Blocking
of **CLN3** expression using Ad-AsCLN3 suppresses growth of
cancer cells. This could be mediated by excess ceramide known to
inhibit cell growth and result in cell cycle arrest.

L4 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1
 ACCESSION NUMBER: 2002099667 MEDLINE
 DOCUMENT NUMBER: 21818590 PubMed ID: 11830536
 TITLE: The **CLN3** gene is a novel molecular target for **cancer** drug discovery.
 AUTHOR: Rylova Svetlana N; Amalfitano Andrea; Persaud-Sawin Dixie-Ann; Guo Wei-Xing; Chang Jerry; Jansen Paul J; Proia Alan D; Boustany Rose-Mary
 CORPORATE SOURCE: Department of Pediatrics, Duke University Medical Center, Durham, North Carolina 27710, USA.
 CONTRACT NUMBER: R01 DK 52925 (NIDDK)
 R02 NS 30170 (NINDS)
 SOURCE: CANCER RESEARCH, (2002 Feb 1) 62 (3) 801-8.
 Journal code: 2984705R. ISSN: 0008-5472.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200203
 ENTRY DATE: Entered STN: 20020207
 Last Updated on STN: 20020307
 Entered Medline: 20020305


AB Juvenile Batten disease is a neurodegenerative disease caused by accelerated apoptotic death of photoreceptors and neurons attributable to defects in the **CLN3** gene. **CLN3** is antiapoptotic when **overexpressed** in NT2 neuronal precursor cells. **CLN3** negatively modulates endogenous ceramide levels in NT2 cells and acts upstream of ceramide generation. Because defects in regulation of apoptosis are involved in the development of **cancer**, we evaluated the expression of **CLN3** on both mRNA and protein levels in a variety of **cancer** cell lines and solid colon **cancer** tissue. We also observed the effect of the blocking of **CLN3** protein expression on **cancer** cell growth, survival, ceramide production, and apoptosis by using an adenovirus-bearing antisense **CLN3** construct. We show that **CLN3** mRNA and protein are **overexpressed** in glioblastoma (U-373G and T98g), neuroblastoma (IMR-32 and SK-N-MC), prostate (Du145, PC-3, and LNCaP), ovarian (SK-OV-3, SW626, and PA-1), breast (BT-20, BT-549, and BT-474), and colon (SW1116, SW480, and HCT 116) **cancer** cell lines but not in pancreatic (CAPAN and As-PC-1) or lung (A-549 and NCI-H520) **cancer** cell lines. **CLN3** is also up-regulated in mouse melanoma and breast carcinoma **cancer** cell lines. We found **CLN3** expression is 22-330% higher than in corresponding normal colon control tissue in 8 of 10 solid colon tumors. An adenovirus-expressing antisense **CLN3** (Ad-AS-**CLN3**) blocks **CLN3** protein expression in DU-145, BT-20, SW1116, and T98g **cancer** cell lines as seen by Western blot. Blocking of **CLN3** expression using Ad-AS-**CLN3** inhibits growth and viability of **cancer** cells. It also causes elevation in endogenous ceramide production through de novo ceramide synthesis and results in increased apoptosis as shown by propidium iodide and JC-1 staining. This suggests that Ad-AS-**CLN3** may be an option for therapy in some **cancers**. More importantly these results suggest that **CLN3** is a novel molecular target for **cancer** drug discovery.



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<div style="border: 1px solid black; padding: 2px;"> Display the complete GeneCard </div> <div style="border: 1px solid black; padding: 2px; margin-top: 5px;"> for this gene (CLN3) </div> <div style="border: 1px solid black; padding: 2px; margin-top: 5px;"> More like this </div>	<div style="border: 1px solid black; padding: 5px;"> <p>Gene: CLN3 = ceroid-lipofuscinosis, neuronal 3, juvenile (Batten, Spielmeyer-Vogt disease) [Locus: 1</p> <p>The following lines in the GeneCard text contribute to matching your query:</p> <ul style="list-style-type: none"> - GENE: CLN3 (ceroid-lipofuscinosis, neuronal 3, juvenile (Batten, Spielmeyer-Vogt disease)) - OMIM: CLN3 gene; CLN3, BTS 607042 Ceroid-lipofuscinosis, neuronal-3, juvenile - MOUSE HOMOLOG: Cln3 (on chromosome 7, 60.40 Apr 08 2003 gbaccs: AK078976 U47106 U6 NM_009907 cM) - SWISSPROT: CLN3 protein (Battenin) (Batten disease protein). - SWISSPROT: GENE: CLN3 OR BTS - SWISSPROT: DISEASE: DEFECTS IN CLN3 ARE A CAUSE OF BATTEN DISEASE (BD) (ALSO K ONSET NEURONAL CEROID LIPOFUSCINOSIS TYPE 3; JNCL), A RECESSIVELY INHERITED NE DISORDER OF CHILDHOOD CHARACTERIZED BY PROGRESSIVE LOSS OF VISION, SEIZURES PSYCHOMOTOR DISTURBANCES. BIOCHEMICALLY, THE DISEASE IS CHARACTERIZED BY LY ACCUMULATION OF HYDROPHOBIC MATERIAL, MAINLY ATP SYNTHASE SUBUNIT C. CLINICA USUALLY FROM 5 TO 10 YEARS OF AGE. NO TREATMENT IS AVAILABLE AND BD IS USUALLY DECADE. THE INCIDENCE IS ESTIMATED AT 1/20000 TO 1/100000 LIVE BIRTH, MAKING IT ONE COMMON NEURODEGENERATIVE DISEASES OF CHILDHOOD. - SWISSPROT: DATABASE: NCL CLN3 -Neural Ceroid Lipofuscinoses mutation db. - SWISSPROT: DATABASE: Mutations of the CLN3 gene -Retina International's Scientific Newsletter - HGMD: 120593 HGMD entry for CLN3 mutations - UNIGENE: Hs.194660 ceroid-lipofuscinosis, neuronal 3, juvenile (Batten, Spielmeyer-Vogt disease sapiens;Mar 24 2003 CLN3 NM_000086 . . . - LITERATURE: 7553855 Isolation of a novel gene underlying Batten disease, CLN3. The Internati Consortium. SP - BLOCKS: PR01315, CLN3 Batten's disease protein (battenin) signature; - RZPD: id-CLN3 - euGenes: Organism=worm WormSymbol=cln-3.1 WormLocation=V 11266193..11268210 WormDes protein like WormSimilarity=40% WormLink=cln-3.1 Organism=worm WormSymbol=cln-3.2 WormLo 5274774..5278702 WormDescription= WormSimilarity=40% WormLink=cln-3.2 Organism=worm Wor 3.3 WormLocation=V 8685663..8688651 WormDescription=intergral membrane protein WormSimilari 3.3 Organism=fly FlySymbol=CG5582 FlyLocation= 75A2 FlyDescription= FlySimilarity=40% FlyLink - HomoloGene: Organism=Rn Symbol= Location= Description= Similarity=98.39 LocusLink= Unigene=33154 GenBank=BE119371.1 Organism=Dr Syr Description= Similarity=71.77 LocusLink= Unigene=104246 GenBank=BG303854.1 Organism=Mm S </div>
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Description=ceroid lipofuscinosis, neuronal 3, juvenile (Batten, Spielmeier-Vogt disease)
Similarity=80.54|LocusLink=12752|Unigene=232156|GenBank=NM_009907.1|Organism=XI|Symbol:
Description=ESTs, Weakly similar to A57219 Batten disease-related protein **CLN3** - human [H.sapier
Similarity=75.65|LocusLink=|Unigene=84969|GenBank=BJ043920.1|

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National Library of Medicine - Medical Subject Headings**2003 MeSH****MeSH Supplementary Concept Data**[Return to Entry Page](#)

Name of Substance	Batten disease protein CLN3
Record Type	C
Registry Number	0
Entry Term	CLN3 gene product, human
Entry Term	CLN3 protein, human
Entry Term	ceroid lipofuscinosis, neuronal 3 protein
Entry Term	CLN3 protein, Batten disease
Entry Term	battenin
Heading Mapped to	<u>*Proteins</u>
Indexing Information	Neuronal Ceroid-Lipofuscinosis
Source	Genomics 1997 Mar 1;40(2):346-50
Frequency	51
Note	base sequence in first source; GenBank U32680; mouse homolog = CLN3 PROTEIN, MOUSE; don't confuse with CLN3 PROTEIN, YEAST
Date of Entry	19970421
Revision Date	20030228
Unique ID	C105199

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